REMARKS

I. Status of the Claims

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

This amendment amends claim 21 and adds new claim 22. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier.

Exemplary support for the amendments to claim 21 is found in the priority document, U.S. Patent No. 5,010,010 ("the '010 patent). Exemplary support for "purified recombinant intact hPTH" is found in the '010 patent at col. 2, lines 1-6; col. 10, lines 23-36; and figure 12. Support for "wherein said microorganism comprises DNA encoding hPTH(1-84)" is found in the '010 patent at col. 3, lines 41-43. Support for "approximately 9000 daltons" is found in the '010 patent at col. 10, lines 30-32. Finally, support for "wherein purified recombinant intact hPTH(1-84) is produced" is found in the '010 patent at col. 10, lines 23-36, and figure 12.

Claim 22 is being added. Exemplary support for newly added claim 22 is found in the '010 patent as described above. Support for "culturing said microorganism to produce a culturing medium containing said PTH" is found throughout the specification. *See, e.g.,* Example 8.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested. Upon entry of this Amendment, claim 21 will remain pending in the application.

II. Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claim 21 is rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner asserts that purification steps needed to enable the claimed invention are not in the claims or specification. Claim 21(c) states that the purified intact hPTH(1-84) migrates as a single band when subjected to gel electrophoresis. However, according to the Examiner, Example 8 and Figure 12 only teach expression in transfected yeast in which two major bands were seen in gel electrophoresis results.

Applicants respectfully disagree with the Examiner. However, to expedite prosecution, Applicants have amended claim 21 to recite "migrates as a band of approximately 9000 daltons when subjected to gel electrophoresis." Exemplary support for this amendment is found in the priority document, U.S. Patent No. 5,010,010, at col. 10, lines 30-32.

A person of ordinary skill in the art, at the time the claimed invention was made, using well known techniques would have been able to devise a purification procedure for purifying the 9000 dalton band on the gel in Figure 12 without undue experimentation, as there were only two bands present on the gel in Figure 12.

Additionally, attached herewith as Exhibit 1 is Høgset et al., *JBC*, *265*(13):7338-7344 (1990). Høgset et al. disclose expression of hPTH(1-84) in *E. coli* involving an expression plasmid where hPTH cDNA is fused to the signal sequence of *Staphylococcus aureus*-protein A. The expression yielded about 1 mg hPTH(1-84)/liter growth medium. *See e.g.*, page 7338, right panel, of Høgset et al. The hPTH(1-84) was purified using techniques well known to those of ordinary skill in the art at the time of the claimed invention (reverse-phase HPLC), as described on page 7340, right panel, of Høgset et al.

The Examiner also asserts that the specification does not provide sufficient enablement for the microorganism in claim 21 to be *E. coli*. However, as discussed above, Høgset et al. discloses expression of hPTH(1-84) in *E. coli* involving an expression plasmid where hPTH cDNA is fused to the signal sequence of *Staphylococcus aureus*-protein A. The expression yielded about 1 mg hPTH(1-84)/liter growth medium. *See e.g.*, page 7338, right panel, of Høgset et al. Thus, the disclosure of Høgset et al. shows that production of purified recombinant intact hPTH in *E. coli* according to the method of claim 21 is enabled.

Moreover, the protein A secretion system used by Høgset et al. was available from 1983, as noted in the references cited by Høgset et al.

Because Applicants' claim 21 is enabled, withdrawal of this ground for rejection is respectfully requested.

III. Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claim 21 is rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite. Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner asserts that the metes and bounds of "substantially pure" are not provided in the specification. Applicants respectfully disagree with the Examiner. However, for the sole purpose of expediting prosecution, Applicants have amended claim 21 by replacing the term "substantially pure" with the term "purified." A person of ordinary skill in the art would know from the statement in part (c)(3) that the PTH is of a pure form, and would thus know what the term "purified" means.

The Examiner asserts that it is not clear what is purified. Applicants respectfully disagree with the Examiner. Part (c) of claim 21 states "purifying said intact hPTH(1-84)." A person of ordinary skill in the art would know that intact hPTH(1-84) is being purified.

Continuing, the Examiner asserts that claim 21 lacks a conclusion. Applicants have amended claim 21 to recite "wherein purified recombinant hPTH is produced."

The Examiner also asserts that the preamble indicates that recombinant protein is produced, but that the claim is directed to purifying intact hPTH. Applicants have amended the preamble of claim 21 to recite "[a] process for the production of purified recombinant intact hPTH..." and have added the following phrase after step (c): "wherein purified recombinant intact hPTH(1-84) is produced."

The Examiner asserts that claim 21 omits essential steps. In particular, the Examiner asserts that in part (b) it is not clear what structure is required to produce intact hPTH in the microorganism. Applicants respectfully disagree with the Examiner. However, to expedite

prosecution, Applicants have amended claim 21(b) to recite that the microorganism comprises DNA encoding hPTH. Exemplary support for this amendment is found in the '010 patent at col. 3, lines 41-43.

The Examiner also asserts that in part (c), it is not clear what is required for purifying. As discussed above, a person of ordinary skill in the art using well known techniques would have been able to devise a purification procedure for purifying the 9000 dalton band on the gel in Figure 12 without undue experimentation. *See e.g.,* Høgset et al. page 7340, right panel.

Finally, the Examiner asks if an isolated homogenous protein is produced or if an intact hPTH in the presence of other forms is produced. Both bands comprise intact hPTH. The band that migrates at approximately 9000 daltons represents intact hPTH and the band that migrates at approximately 16,000 represents intact hPTH (1-84) fused to its secretion signal. *See e.g.,* Example 8. It is clear from Figure 12 and Example 8 that intact hPTH is produced. However, to expedite prosecution, Applicants have amended part (c) of claim 21 to state that the purified hPTH "migrates as a band of approximately 9000 daltons when subjected to gel electrophoresis." Therefore, a person of ordinary skill in the art would know that the hPTH is purified hPTH.

As Applicants' claim 21 is definite, withdrawal of this ground for rejection is respectfully requested.

IV. Issues Under Double Patenting

Claim 21 is rejected by the Examiner under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1, 26-28, and 11 of U.S. Patent No. 6,146,852 ("the '852 patent").

Attached herewith is a terminal disclaimer which disclaims the terminal part of the term of any patent granted on the above identified patent application which would extend beyond the full statutory term of the '852 patent. This ground for rejection is now moot.

Claim 21 is also provisionally rejected by the Examiner under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 33-35 of copending Application No. 08/340,664 ("the '664 application"). Applicants respectfully request the Examiner to hold this rejection in abeyance until claims are allowed in the present application or in the '664 application.

V. New Claim 22

Applicants have added new claim 22 to further define claim scope. Applicants' arguments related to claim 21 apply equally to new claim 22. Therefore, claim 22 is in condition for allowance.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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